



EMA-CMDv-70466-2006
London, 16 March 2007

ANNUAL REPORT 2006

7 Westferry Circus
Canary Wharf
London E14 4HB
United Kingdom

CONTENTS

1	Introduction.....	2
2	Members	2
3	Meetings.....	2
4	Authorisation procedures.....	3
5	Policy issues.....	5
5.1	SPC harmonisation	5
5.2	Generic products	5
5.3	Diluents	5
5.4	Environmental risk assessment.....	6
5.5	Labelling.....	6
5.6	Other issues	6
6	Quality management	7
7	Co-operation with other groups	8
8	Stakeholders	9
9	The secretariat	9
	Annex I List of abbreviations.....	10
	Annex II Members, observers and the secretariat	11

1 Introduction

This is the first annual report of the veterinary Co-ordination group for Mutual recognition and Decentralised procedures, CMD(v), and it covers the period from the establishment of the group on 30 October 2005, until the end of 2006. The report provides an overview of, and reflects on, the work carried out. Any follow-up actions are included in the work plan 2007 and/or will be included in future meeting agendas.

CMD(v) has been established under the revised EU pharmaceutical legislation¹ for the examination of any question relating to marketing authorisation of a medicinal product in two or more Member States, in accordance with the mutual recognition procedure (MRP) or the decentralised procedure (DCP). The group adopted a logo and proposed its Rules of Procedure. The European Commission endorsed the Rules of Procedure, after which they were published on the Heads of Medicines Agencies website (www.hma.eu).

An explanatory list of abbreviations used in this report, is provided in Annex I.

2 Members

At the start of CMD(v), the competent authority from each country in the European Economic Area (EEA) nominated one member. The members elected from their midst Esther Werner as chairperson for a period of 3 years. The vice-chairpersons during the UK, Austrian and Finnish presidencies of the Council of the European Union were, respectively, Gavin Hall, Eugen Obermayr and Paula Kajaste.

A representative from the European Commission attended the meetings. An observer from acceding Member State Bulgaria also attended the meetings.

Members from Austria, Estonia, Iceland, Latvia, the Netherlands, Norway, Poland and Spain were replaced in the course of the year 2006. A full list of members and observers is provided in Annex II. The list of CMD(v) members, including their professional qualification, has been published on the Heads of Medicines Agencies website.

3 Meetings

CMD(v) held monthly meetings at the European Medicines Agency (EMA) in London, except for the month of August. Meetings were scheduled on Thursday and Friday, directly after the meeting of the Committee for Medicinal Products for Veterinary Use (CVMP). Sub-Groups regularly met prior to the main plenary session to discuss specific issues such as Document Management, the joint CMDv / IFAH-Europe Survey, SPC harmonisation and Diluents. During the plenary sessions CMD(v) addressed policy issues, questions from industry and Member States and the development of the document management system. Discussions were held on procedures reaching day 78, day 198 and day 50 for products going through MRP,

¹ Article 31 of Directive 2001/82/EC as amended by 2004/28/EC

DCP and referral procedures respectively. Company hearings were conducted in the framework of referral procedures. Regular meetings were held with industry representative organisations, IFAH-Europe and EGGVP, to discuss regulatory issues.

The Finnish presidency organised an informal meeting in Helsinki on 4 and 5 September. At this meeting the CMD(v) discussed labelling proposals from industry, national requirements for the blue box (chapter 7 of the NtA) and the experience gained with the 60 day referral procedure and the decentralised procedure. In a joint session with CVMP the communication between the two groups was discussed. Also discussed were ways to reduce the number of referrals and the issues regarding diluents. CMD(v) was also informed about the European Surveillance Strategy, the work of the Task Force on availability and the conduct of the MRP in Finland.

All Member States, except for Iceland, Liechtenstein, Luxembourg and Malta participated in CMD(v) meetings.

4 Authorisation procedures

The core business of CMD(v) is to facilitate a smooth conduct of the MRP and DCP and in particular to consider points of disagreement, raised by Member States in relation to the assessment report, summary of product characteristics (SPC), labelling and package leaflet of a veterinary medicinal product, on the grounds of potential serious risk to human or animal health or to the environment.

The CMD(v) discussed and acknowledged the publication by the European Commission of the "Guideline on the definition of a potential serious risk to human or animal health or for the environment" in the context of Article 33(1) and (2) of Directive 2001/82/EC, as amended.

MRP takes 90 days and DCP 210 days. If CMD(v) fails to reach an agreement at day 90/210, because one or more Member States believe the product is a potential serious risk to human or animal health or to the environment, a 60 day referral CMD(v) procedure is initiated. If the Member States included in the procedure cannot reach an agreement at day 60 of the referral, the matter is referred to CVMP for arbitration.

The number of products and procedures (in brackets) CMD(v) dealt with, are stated in table 1 on the next page. To enable future comparison with following calendar years, separate information for the calendar year 2006 has been included.

It should be noted that the presented numbers of started and finalised procedures are not directly linked. Started procedures may not have ended at the end of 2006, while finalised procedures may have started before 30 October 2005.

CMD(v) discussed all procedures at day 78/198 at the meeting where more than two concerned Member States were involved and major concerns were outstanding. About 1 out of 4 of the products in MRP and DCP was an immunological.

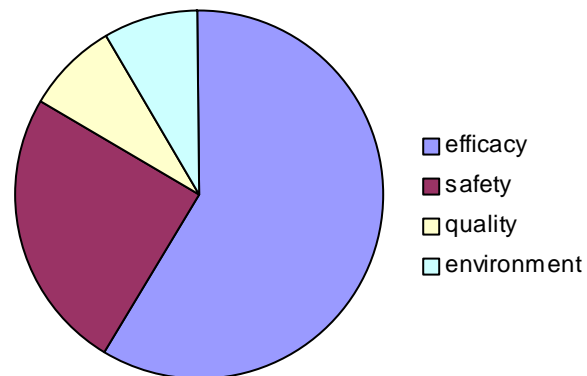
	Started	reached day 90 / 210	referred to CMD(v)	resolved	pending 31/12/07	referred to CVMP
30/10/2005 – 31/12/2006						
MRP	98 (122)	88 (111)	11	4	1	6
DCP	26 (30)	4 (4)	1	0	1	0
Total	124 (152)	92 (115)	12	4	2	6
01/01/2006 – 31/12/2006						
MRP	77 (99)	70 (91)	8	4	1	6
DCP	25 (29)	4 (4)	1	0	1	0
Total	102 (128)	74 (95)	9	4	2	6

Table 1. MRP, DCP and referrals

Twelve products (related to 16 procedures) were referred to CMD(v) as no agreement was reached at day 90/210 of the procedure. Two of them were immunologicals. The area of disagreement, as depicted in graph 1, related to efficacy in 7 cases, to safety for the animal in 3 cases, to product quality in one case and to safety for the environment in one case.

Disagreement was caused by:

- dossiers not meeting current standards, in particular with regard to efficacy;
- differences between the reference product authorised in the Member States;
- divergent national policies on safety and quality.



Graph 1. Main areas of disagreement

Following the informal meeting in Helsinki, CMD(v) encouraged members states and industry to discuss prior to submission the quality of the dossier and the chances of a successful procedure.

CMD(v) could not reach an agreement finally on 6 products, representing 50% of the CMD(v) referrals and 6.5% of all products that reached day 90/210. These products were referred to CVMP for arbitration. By the end of 2006, CVMP had delivered an opinion on 2 products, with the recommendation to maintain the marketing authorisations, whilst 4 arbitration procedures were ongoing.

5 Policy issues

In relation to the implementation of Directive 2004/28/EC and following questions from industry and competent authorities, discussions were held to devise or amend policies regarding product harmonisation, generics, diluents, environmental risk assessment and harmonisation of labelling requirements.

5.1 SPC harmonisation

By 30 April 2005, 4 Member States had submitted a list of in total 82 veterinary medicinal products, proposed for harmonisation, in accordance with article 34(2) of Directive 2001/82/EC. An ad hoc subgroup was set up and chaired by Eugen Obermayr, to scrutinise the products and to advise CMD(v) on a list for harmonisation, to be presented to the European Commission.

Within 4 months the subgroup reported to CMD(v) that none of the proposals would help to achieve the objectives of the Directive. It was considered that a harmonisation exercise could jeopardise rather than improve the availability of veterinary medicines. Harmonising different SPCs based on old dossiers, could easily lead to loss of indications, target species or complete products, while the Member States were keen to keep them in the local market. No serious safety concerns requiring harmonisation were identified and it was noted that other legal provisions would be equally or more adequate to tackle serious safety concerns should they emerge.

CMD(v), including the 4 Member States who submitted the initial proposals, endorsed the subgroup's conclusions, with one abstention from voting and agreed not to forward a list of products for harmonisation to the European Commission.

5.2 Generic products

Various questions regarding regulatory issues with generic products were received from industry through the website, directly by e-mail or via a Member State. Question and answer documents were published on the website.

CMD(v) also considered how to deal with generic applications, where the generic has more indications, more target species or shorter withdrawal periods than the reference product in a Member State. An additional claim may be substantiated by data provided by the applicant. However, where an additional claim is based on the originator product authorised in the Reference Member State, Member State appeared to differ in the extent they wish to assess supporting data of the originator product. There were also concerns as to how the marketing authorisation holder of an originator product can maintain parity with the generic.

Although all Member States agreed that in principle a generic can have a different SPC from the reference product in a Member State, no conclusions on a harmonised approach were reached by the end of 2006 and CMD(v) requested the Heads of Medicines Agencies for guidance.

5.3 Diluents

Validation of MRP and DCP applications, revealed that Member States handle products including diluents differently. Some Member States handle a product, which may be used with more than 1 diluent, in one single procedure. Others require a separate procedure for each diluent/active combination.

The differences have led to severe delays to the start of a small number of procedures. CMD(v) showed however its commitment to find a solution. The HMA, who were informed about the matter, urged CMD(v) to find a pragmatic and flexible solution, in the interest of medicine availability. Intensive discussions continued until the end of 2006, at which point it was decided to set up an ad hoc subgroup to resolve the issue.

5.4 Environmental risk assessment

New requirements with regard to environmental risk assessment were introduced with Directive 2004/28/EC. Members of the group contributed at the request of EMEA to the CVMP reflection paper in the implementation of environmental risk assessment. CMD(v) endorsed the paper. Further guidance from the European Commission regarding the practical implementation of the new legislation was awaited.

In the mean time, the first product was referred to CMD(v) over environmental concerns. These concerns related to the toxicity to plants, persistence in soil and leaching to the groundwater. Agreement was reached during the CMD(v) referral procedure to grant a marketing authorisation for the product, on the basis that the product's use was restricted in the SPC and risk mitigation measures were included in the product literature.

5.5 Labelling

Industry noted several regulatory problems with labelling and IFAH-Europe addressed these at a workshop in Prague in spring 2006. As follow up, the CMD(v) in collaboration with the Quality Review of Documents group conducted a survey, led by Christophe Debruyne, to investigate current practices as well as the feasibility of proposed resolutions. By the end of 2006, the outcome of the survey indicated that:

- Member States would accept the submission of mock ups in 3x English language to test the available space;
- Lot could be used for batch and exp for expiry date on small labels;
- Pictograms of animals could be used as a supplement;
- Pictograms of animals would not be accepted as a replacement for text;
- 150 ml could not be accepted as a small vial.

For other issues the Member States' positions were not harmonised and it was decided to continue discussions in 2007 to find an agreed approach where possible.

5.6 Other issues

In addition to the issues mentioned above further questions were discussed concerning variations, validation criteria for procedures, GMP for active ingredients, starting materials of biological origin, stability data, nosodes, bibliographical applications, withdrawal periods, veterinary diagnostics, licensing of pure substances, renewals and repeat use procedures.

6 Quality management

To ensure a consistent and accurate conduct of activities, CMD(v) developed a number of management and operating procedures as well as best practice guides, which now form a comprehensive document management system. Much of the preparatory work was carried out by a subgroup chaired by Dolores Sandoval. Industry has been consulted on various documents.

Published documents include:

- Rules of procedure for CMD(v)
- Standard operating procedure for referral to CMD(v) and oral explanation
- Best practice guide for
 - MRP
 - DCP
 - repeat use of MRP and DCP
 - Type IA variations
 - Type IB variations
 - Type II variations
 - Renewals
 - Automatic validation of MRP
 - Processing of SPC, labelling and packaging provide in support of MRP and DCP
 - Active substance master file in the MRP and DCP + variation procedures, for restricted parts
 - Contacts with representative organisations
- Guidance document for
 - Contact points for general inquiries – public access
 - Clock start dates
 - Documentation to be submitted by a Member State when the veterinary medicinal product is not authorised in the Member State
 - Geographical origin of biological starting materials
- CMD(v) annotated QRD template

Further documents were elaborated by the group to be able to comply with the functions established in the Directive and the Rules of procedure as well as to ensure the effective functioning of the CMD(v).

The group has developed a proposal for the structure for the CMD(v) part of the new Head of Agencies website.

7 Co-operation with other groups

CMD(v) maintained contacts with other groups in the regulatory field to co-ordinate activities of mutual interest.

The CMD(v) chairperson updated HMA on a regular basis at their meetings and addressed to HMA questions regarding diluents and generics. She also provide CMD(v) with feedback from the HMA meetings.

Agendas and minutes were exchanged and monthly oral reports given to and received from CVMP. Dedicated meetings were organised with the chairpersons and secretariats to discuss areas of common interest, such as referral procedures and advice from working parties. The chairpersons' meeting was in the course of 2006 replaced by CMD(v) participation in the CVMP Strategic Planning Group.

Also with CMD(h) agendas and minutes were exchanged, as well as monthly oral reports were given and received. CMD(v) took particular interest in discussions on policy issues, e.g. regarding generics, and in documents developed by CMD(h). Several documents were used as a basis for the development for veterinary documents as a matter of efficiency and consistency.

Contacts with the veterinary pharmacovigilance working party (PhvWP) developed over time, especially after the mandate of the working party was extended to non-centralised procedures. The group took note of the agenda's and minutes of the PhvWP. The PhvWP chairperson and secretariat presented the latest developments at the CMD(v) meetings. The development of a SOP on EU crisis management for mutually recognised and national authorised products was requested by HMA to CMD(v) and PhvWP.

After the extension of the PhvWP mandate, areas of mutual interest and possible future co-operation were identified as:

- work sharing on PSUR assessments and harmonisation of international birth dates;
- SPC texts relating to adverse reactions and user safety;
- Description of pharmacovigilance systems that MAHs need to put/have in place;
- Results of pharmacovigilance inspections for MRP/DCP;
- Post authorisation surveillance studies on safety as condition for authorisation.

In the field of information technology, CMD(v) members were represented in CTS user group and TIGes-v. CTS is a very important communication tool and database, for the functioning of MRP and DCP in the veterinary and human fields. The system has been subject to continuous development.

CMD(v) was also represented in the EMEA TIGes-v group on e-submission. In this group authorities and industry discussed the policy on and technical possibilities of electronic submission.

8 Stakeholders

Contacts with industry representative organisations, IFAH-Europe and EGGVP, have been maintained and meetings were conducted in March, June and October. At those meetings a variety of regulatory issues were addressed, including:

- CMD(v) best practice guides under consultation;
- The IFAH-Europe – CMD(v) survey;
- IFAH-Europe packaging proposals;
- EGGVP questions regarding the eligibility generic application constructions;
- Diluents for vaccines;
- The number of referrals and ways to reduce the unnecessary ones;
- The CMD(v) position on requirements for starting materials of biological origin;

By the end of the year 2006 it was proposed to extend the contacts in future to other stakeholders, such as:

- AVC, association of veterinary consultants
- FVE, the European Federation of Veterinarians
- and COPA-COGECA, a European organisation representing farmers.

Together with IFAH-Europe the survey regarding the survey report on the MRP in 2005 was finalised. The survey on MRP, DCP and referrals in 2006 was carried out. A subgroup was set up and chaired by Christophe Debruyne, to facilitate a smooth conduct of the survey. The conclusions of the 2005 survey underlined the importance of MRP to market veterinary medicinal products in the EEA.

9 The secretariat



supported CMD(v) with a secretariat by preparing and hosting the meetings in London, conducting follow up to meetings, archiving and providing advice. The secretariat distributed meeting documents in 2 mailings prior to and 1 mailing after each meeting. Agendas were reorganised and hyperlinked to enhance the efficiency of the meetings and in preparation of a move toward paperless meetings by 1 January 2007. Of each meeting the secretariat prepared minutes, a list of actions and a report for public release. For the referral procedures the secretariat drew up timetables, notified the applicants, provided them with the list of questions and organised hearings, 7 in total.

Secretarial support was also given to the subgroup for SPC harmonisation and the subgroup for document management.

The secretariat has played a facilitating role in supporting the work of the group to find pragmatic solutions to the intractable issues related to diluents and packaging.

The secretariat liaised closely with the CVMP, CMD(h) and PhvWP secretariats as well as maintaining contacts with the national agencies, IFAH-Europe, EGGVP and other stakeholders.

Annex I List of abbreviations

CMD(h)	Coordination group for Mutual recognition and Decentralised procedures (human)
CMD(v)	Coordination group for Mutual recognition and Decentralised procedures (veterinary)
CTS	Communication and Tracking System
CVMP	Committee for Medicinal Products for Veterinary use
DCP	Decentralised Procedure
EEA	European Economic Area (= EU+Iceland+Norway+Liechtenstein)
EMA	European Medicines Agency
HMA	Heads of Medicines Agencies
MRP	Mutual Recognition Procedure
MAH	Marketing Authorisation Holder
MS	Member State
NtA	Notice to Applicants
PhvWP	Pharmacovigilance Working Party
SPC	Summary of Product Characteristics
TIGes-v	Telematics Implementation Group E-Submissions veterinary

Annex II Members, observers and the secretariat

Name	Representing	Function
Esther Werner	CMD(v)	chairperson
Johannes Dichtl	Austria	member (11-12 2005)
Eugen Obermayr	Austria	member (01-12 2006) vice-chairperson (01-06 2006) chairperson SPC subgroup
Christophe Debruyne	Belgium	member chairperson survey subgroup
Maria Papaprodromou	Cyprus	member
Daniel Dušek	Czech Republic	member
Asbjørn Brandt	Denmark	member
Triin Teppor	Estonia	member (replaced)
Helen Mahla	Estonia	member
Paula Kajaste	Finland	vice chairperson (07-12 2006) chairperson NtA subgroup
Laëtitia Le Letty	France	member
Gabriele Schweyen	Germany	member
Ioannis Malemis	Greece	member
Gábor Kulscár	Hungary	member
Halldør Runólfsson	Iceland	member (replaced)
Inga Pálsdóttir	Iceland	member
Maggie Gething	Ireland	member
Virgilio Donini	Italy	member
Valda Sejane	Latvia	member (replaced)
Renate Kuske	Latvia	member
Peter Malin	Liechtenstein	member
Kristina Sudikienė	Lithuania	member
Marc Wirtor	Luxembourg	member
Kenneth Mifsud	Malta	member
José Jonis	Netherlands	member (replaced)
Trudy Knol	Netherlands	member
Tove Bjerknes	Norway	member (replaced)
Tora Gauslaa	Norway	member
Michał Pochodyła	Poland	member (replaced)
Agata Dyrkacz	Poland	member
Margarida Alves	Portugal	member
Judita Hederová	Slovakia	member
Katarina Štraus	Slovenia	member
Dolores Sandoval	Spain	member (replaced) chairperson documentation subgroup
Carmen Sanchez	Spain	member
Vera Franzén	Sweden	member
Gavin Hall	United Kingdom	member vice chairperson (11-12 05)
Karin Krauss	European Commission	observer
Ilian Getchev	Bulgaria	observer
Maria Szábo	EMEA CMD(v) secretariat	CMD(v) secretary (replaced)
Wim Riepma	EMEA CMD(v) secretariat	CMD(v) secretary
Veronica Picciafuoco	EMEA CMD(v) secretariat	administrative assistant
María Blanca Gómez	EMEA CMD(v) secretariat	secretarial assistant